Remarks

Status of the Claims and Support for the Amendments to the Claims

By the foregoing amendments, claims 3-5, 7-10, 12-14 and 16-18 are sought to be amended. Claims 1, 2 and 6 have been cancelled without prejudice or disclaimer. New claims 20-25 are sought to be added. Applicants retain the right to pursue the subject matter of the canceled claims in one or more divisional or continuation patent applications.

Support for the amendments to claims 3-5, 7-10, 12-14 and 16-18 can be found throughout the present specification and in original claims 1-9. Support for new claims 20-25 can be found in the present specification at pages 4-6. Therefore, these amendments introduce no new matter.

Upon entry of the foregoing amendments, claims 3-5, 7-10, 12-14 and 16-25 are pending in the application with claims 3, 7, 20 and 23 being the independent claims. Claims 10-19 have been withdrawn from consideration by the Examiner.

Summary of the Office Action

In the Office Action dated February 6, 2008, the Examiner has made two rejections of the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

Rejection under 35 U.S.C. § 103(a) over Venkataraman

In the Office Action at pages 4-6, the Examiner has rejected claims 1-9 under 35 U.S.C. § 103(a), as allegedly being unpatentable over Venkataraman (US 6,509,492 B1; hereinafter "Venkataraman"). Applicants respectfully traverse this rejection.

The Examiner contends that Venkataraman discloses a composition for treating upper respiratory indications comprising combinations of an antihistamine, an antitussive and an expectorant. The Examiner further contends that Venkataraman discloses antihistamines such as pyrilamine tannate; decongestants such as phenylephrine tannate; and expectorants such as guaifenesin tannate. Office Action at page 5, second paragraph.

The Examiner states that "Venkataraman does not specifically teach the exact amounts of each compound as disclosed in claims 3-5 and 7-9." Office Action, page 5, third paragraph. The Examiner alleges that one of ordinary skill in the art at the time of filing of the present invention would have found it obvious to have utilized the amounts of each active ingredient as disclosed in original claims 3-5 and 7-9 in the compositions of Venkataraman, because Venkataraman allegedly discloses ranges that either overlap or are close to Applicants' amounts. The Examiner further alleges that the following observations provide motivation for selecting the presently claimed amounts of active ingredients:

> (1) the Applicant's claim language "about"; (2) the suggested dosage amounts provided by Venkataraman are not to be seen as limiting . . . ; (3) maximum dosages for both adults and children are given by Venkataraman . . . which means that the hourly dosages can be adjusted . . . ; and (4) it is the normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.

Office Action at page 6, lines 7-15. In support of point (4) above, the Examiner cites three cases, *In re Boesch*, 617 F.2d 272 (CCPA 1980); *In re Baird*, 16 F.3d 380 (Fed. Cir. 1994); and *In re Jones*, 958 F.2d 347 (Fed. Cir. 1992). Applicants respectfully disagree with the Examiner's contentions and conclusions noted above and submit that the cases cited by the Examiner do not support the asserted conclusions.

Present claim 3 (and hence, claims 4 and 5 that depend ultimately therefrom) recites a therapeutic composition in tablet form for the symptomatic relief of cough and nasal decongestion associated with adverse respiratory tract conditions in warm-blooded animals in need of such treatment, the composition comprising pharmaceutically effective amounts of active ingredients, wherein the active ingredients consist of 20 to 30 mg of phenylephrine tannate, 40 to 80 mg of pyrilamine tannate, and 100 to 400 mg of guaifenesin.

Present claim 7 (and hence, claims 8 and 9 that ultimately depend therefrom) recites a therapeutic composition in suspension form for the symptomatic relief of cough and nasal decongestion associated with adverse respiratory tract conditions in warm-blooded animals in need of such treatment, the composition comprising pharmaceutically effective amounts of active ingredients, wherein the active ingredients consist of 3 to 15 mg of phenylephrine tannate, 25 to 35 mg of pyrilamine tannate, and 50 to 300 mg of guaifenesin, per 5 ml of suspension.

"Under § 103, the scope and content of the prior art is to be determined; differences between the prior art and the claims at issue are to be ascertained; and the

level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined." *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17 (1966). Applicants respectfully submit that the differences between the presently claimed invention and Venkataraman are so great that it would not have been obvious to modify the disclosure of Venkataraman in order to make and use the presently claimed invention.

As noted by the Examiner at page five of the Office Action, Venkataraman does not disclose the specified amounts of each active ingredient as recited in the present claims. Applicants respectfully submit, as discussed in detail below, the ranges of the various active agents disclosed in Venkataraman are so broad that there could be no predictability in selecting the amounts of active agents so as to render obvious the presently claimed invention. *See, KSR Int'l. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) ("a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions."). Applicants respectfully submit that it would not have been predictable that the ranges specified in present claims would have been therapeutically effective based simply on the broad ranges of active ingredients disclosed in Venkataraman. Thus, Applicants respectfully submit that a person of ordinary skill in the art would not look to modify the disclosure of Venkataraman, so as to select the amounts of active agents specified in the present claims, as such a modification would not have yielded predictable results.

Regarding the Examiner's point (1) above, Applicants respectfully submit that the use of the term "about" in the claims fails to provide any motivation to select the claimed

ranges, or renders the claims of the present invention obvious. Applicants respectfully submit that Venkataraman does not disclose a therapeutic composition in tablet form, or in suspension form, comprising active ingredients consisting of phenylephrine tannate, pyrilamine tannate and guaifenesin at the amounts recited in the present claims. Use of the term "about" in the claims does not provide any additional motivation or *predictability* to guide a person of ordinary skill in the art to select the ranges or amounts specified in the present claims from the broad ranges disclosed in Venkataraman.

Regarding rationale (2) above, Applicants respectfully disagree with the Examiner that the suggested dosage amounts provided by Venkataraman are not to be seen as limiting. Venkataraman fails to provide *any* guidance for choosing dosage amounts other than those specifically disclosed in the reference. For example, Tables 2 and 3 of Venkataraman only disclose representative dosages of active agents as single therapeutic agents. Furthermore, only two of the three presently claimed active ingredients (pyrilamine maleate/tannate and guaifenesin) are indicated. Neither Table 2 nor Table 3 of Venkataraman disclose specific representative dosages of phenylephrine tannate, nor are active ingredient dosages for a therapeutic composition comprising all three active ingredients of the presently claimed invention disclosed in Venkataraman.

Table 4 of Venkataraman discloses only extremely broad preferred ranges of stand-alone active ingredients with no guidance as to the selection of more narrowly preferred dosages for any of the presently claimed active agents. For example, Table 4 discloses a preferred daily dose range of guaifenesin that spans nearly three orders of magnitude (e.g. 5 to 3000 mg/day). Table 4 of Venkataraman discloses similarly broad

ranges for both pyrilamine maleate and phenylephrine tannate that span 200-fold and 160-fold concentration ranges, respectively.

While Table 5 appears to disclose preferred dosages of active ingredients for combinatorial liquid formulations, it does so only for liquid formulations of guaifenesin in combination with pseudoephedrine tannate. Phenylephrine tannate and pyrilamine tannate are not even included in the "most preferred" liquid formulations. Hence, Table 5 of Venkataraman fails to provide any guidance as to preferred dosages for two of the three active ingredients of the presently claimed therapeutic compositions.

Thus, Applicants submit that the Examiner's contention that a person of ordinary skill in the art would have been motivated to select the amounts of each active agent as recited in the present claims (*see* Office Action at page 6, lines 1-4) can only be based on Applicants' own disclosure and impermissible hindsight. *See* M.P.E.P. § 2145(X)(A). As the Federal Circuit has held numerous times, such a hindsight-based analysis is impermissible. *See, e.g., Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1143 (Fed. Cir. 1985) ("When prior art references require selective combination by the [fact-finder] to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself."); and *In re Pleuddemann*, 910 F.2d 823, 828 (Fed. Cir. 1990) (noting that use of an applicant's specification as though it were prior art to support an obviousness determination is legal error). The Board of Patent Appeals and Interferences has also provided the same mandate on this issue:

> it is impermissible to use the claimed invention as an instruction manual or "template" to piece together isolated disclosures and teachings of the prior art so that the claimed invention may be rendered obvious . . . . a

> rejection based on § 103 must rest on a factual basis, with the facts being interpreted without hindsight reconstruction of the invention from the prior art. In making this evaluation, the examiner has the initial duty of supplying the factual basis for the rejection he advances. He may not, because he doubts that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in the factual basis.

Ex parte Haymond, 41 USPQ2d 1217, 1220 (Bd. Pat. App. Int. 1996). The Court in *KSR* also cautioned against the use of hindsight in support of an obviousness rejection. *See* 127 S.C.t at 1742 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant on *ex post* reasoning."). Thus, the use of hindsight analysis in the present case is impermissible and cannot be used to attempt to establish a *prima facie* case of obviousness.

Applicants further submit that the courts have long held that the disclosure of a genus does not necessarily provide support for every species or subgenus within the genus. *See In re Ruschig*, 379 F.2d 990, 996, 154 USPQ 118, 121-23 (CCPA 1967); *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996); *see also Purdue Pharma L.P. v. Faulding Pharma. Co.*, 230 F.3d 1320, 1326-27 (Fed. Cir. 2000). The CCPA analogized the determination of whether the disclosure of a genus adequately describes a species to trying to follow a trail through the woods, and provided the following illustration in *In re Ruschig*:

> It is an old custom in the woods to mark trails by making blaze marks on the trees. It is no help in finding a trail or in finding one's way through the woods where the trails have disappeared--or have not yet been made, which is more like the case here--to be confronted simply by a large number of unmarked trees. Appellants are pointing to

> trees. We are looking for blaze marks which single out particular trees. We see none.

379 F.2d at 994-95, 154 USPQ at 122; *see also Purdue Pharma.*, 230 F.3d at 1326-27; *Fujikawa*, 93 F.3d at 1570, 39 USPQ2d at 1905. In considering whether the specification provides sufficient guidance to select a species from a broad genus, a court will look to see whether the disclosure narrows the selection of the possible values for the variables in the generic disclosure.

The standard in *Ruschig* is not limited to only cases involving claims to chemical compounds. Rather, this standard may be applicable in other situations where generic disclosure is relied upon to support claims directed to specific subject matter. It has, for example, also been applied to determine whether a given limitation in a pharmaceutical formulation claim was adequately described. *See e.g., Purdue Pharma.*, 230 F.3d at 1226-27 ("Although this case differs from *Ruschig* in that what was disclosed in *Ruschig* was a genus encompassing potentially half a million compounds, the rationale applies equally to this case, in which the disclosure of the [patent at issue] discloses a multitude of pharmacokinetic parameters, with no 'blaze marks' directing the skilled artisan to the C_{max}/C_{24} ratio or what value that ratio should exceed.")

Applicants note that the Examiner specifically stated that "Venkataraman does not specifically teach the exact amounts of each compound as disclosed in claims 3-5 and 7-9 [of the original claims]". Office Action, page 5, last two lines. In view of *Ruschig*, Applicants submit that Venkataraman fails to provide the required rationale, -- *i.e.*, it does not provide the necessary "blaze marks" -- for selecting the combination of dosages of *any* of the three active ingredients in the present claims from the broad ranges

disclosed in Venkataraman. Hence, under *Ruschig*, Venkataraman does not disclose or suggest the presently claimed compositions or methods.

Regarding the Examiner's point (3) above, even assuming *arguendo* that the hourly dosages can be adjusted to compensate for age differences, there still exists a lack of disclosure and guidance as to the selection of a specific dosage for any of the three individual active ingredients in the presently claimed invention, as set forth above, and as required under *Ruschig*. 379 F.2d at 994-95. Hence, under *Ruschig*, Venkataraman does not disclose or suggest the presently claimed compositions or methods.

Regarding the Examiner's point (4) above, Applicants disagree that the "normal desire of scientists and artisans to improve upon what is already generally known" provides the required motivation to determine the combination of active ingredients recited in the present claims. Venkataraman fails to provide any guidance as to the selection of preferred dosages for any of the three claimed active ingredients beyond only very broad concentration ranges. Applicants further submit that the cases cited in the Office Action do not support the Examiner's conclusions.

Regarding *Jones*, Applicants note that the court in that case explicitly stated that "[w]e *decline* to extract from *Merck* the rule that the solicitor appears to suggest - that regardless of how broad, a disclosure of a chemical genus *renders obvious any species* that happens to fall within it." 958 F.2d at 350 (emphasis added). *Baird* similarly held that "[t]he fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious." 16 F.3d at 382. Lastly, Applicants submit that the CAFC affirmation of obviousness in *Boesch* can be

distinguished from the present case. In *Boesch,* the court clearly noted the presence of guidance and predictability as being important to the decision that selection of an optimum value from a broad range would have been obvious. *See, e.g.,* 617 F.2d at 276 ("We are persuaded that one of ordinary skill in the art *would have been guided by these principles*." (emphasis added)). As discussed above, such evidence of guidance and predictability does not exist in Venkataraman.

In summary, Applicants respectfully submit that the ranges of active ingredients disclosed in Venkataraman are so broad that a person of ordinary skill in the art would have not been able to select the ranges and/or precise amounts of the active ingredients recited in the present claims with any level of predictability as to their therapeutic effectiveness. Lack of such predictability can be evidence of non-obviousness. *See, KSR,* 127 S.Ct. at 1740. Furthermore, it is only based on impermissible hindsight using Applicants' own specification that one of ordinary skill would even have been directed to select the presently claimed ranges. As the Federal Circuit has held numerous times, such a hindsight-based analysis is impermissible. *See, e.g., Interconnect Planning Corp.* 774 at 1143. Finally, as the Federal Circuit has also held, the disclosure of a genus does not necessarily provide support for every species or subgenus within the genus, and a generic disclosure must narrow the selection of possible values for the variables. *See In re Ruschig*, 379 F.2d at 996; *Fujikawa*, 93 F.3d at 1571; *see also Purdue Pharma*, 230 F.3d at 1326-1327. Thus, Applicants respectfully submit that a person of ordinary skill in the art would not have selected the amounts of active ingredients set forth in the present claims, and hence, the Examiner has not set forth a *prima facie* case of obviousness.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Rejection For Obviousness-type Double Patenting

The Examiner has also rejected claims 1-9 for obviousness-type double patenting as allegedly being unpatentable over claims 1-3 and 7-10 of Dang *et al.*, U.S. Patent No. 6,462,094 B1 (herinafter "Dang") in view of Venkataraman (US 6,509,492 B1). Applicants respectfully traverse this rejection.

The Examiner contends that Dang discloses a therapeutic composition for the symptomatic relief of cough comprising pharmaceutically effective amounts of active ingredients consisting of phenylephrine tannate and guiafensin in tablet and suspension form. The Examiner states that Dang does not disclose pyrilamine tannate or its amounts. In order to cure this deficiency, the Examiner relies on the disclosure of Venkataraman, alleging that it would have been obvious to combine the composition of Dang with the disclosure of pyrilamine tannate from Venkataraman so as to render the present invention obvious. Applicants respectfully disagree with the Examiner's conclusions.

As set forth in detail above, Applicants respectfully submit that the range of pyrilamine tannate disclosed in the compositions of Venkataraman is so broad (preferred amounts span a 200-fold concentration range) that a person of ordinary skill in the art would have not been able to select the amount of this active ingredient as set forth in the present claims with any level of predictability as to their therapeutic effect. *See, KSR,*

127 S.Ct. at 1740, noting obviousness must be based on a predictable use of known elements. Furthermore, Applicants submit that it is only based on impermissible hindsight that one of ordinary skill would even be directed to select the amount of pyrilamine tannate recited in the presently claimed compositions. As the Federal Circuit has held numerous times, such a hindsight-based analysis is impermissible. *See, e.g., Interconnect Planning Corp.* 774 at 1143. Finally, as the Federal Circuit has held, the disclosure of a genus does not necessarily provide support for every species or subgenus within the genus, and a generic disclosure must narrow the selection of possible values for the variables. *See In re Ruschig*, 379 F.2d at 996; *Fujikawa*, 93 F.3d at 1571; *see also Purdue Pharma*, 230 F.3d at 1326-1327. Thus, Applicants respectfully submit that a person of ordinary skill in the art would not have selected the amount of pyrilamine tannate set forth in the presently claimed compounds for use in the compositions of Dang.

Hence, Applicants respectfully disagree that the presently claimed invention is rendered obvious under the doctrine of non-statutory double patenting over Dang in view of Venkataraman. Reconsideration and withdrawal of this rejection are respectfully requested.

Request For Rejoinder Under 37 C.F.R. § 1.104

Applicants respectfully request that withdrawn claims 10-19 be rejoined in this application and that all of the claims be fully examined for patentability in accordance with 37 C.F.R. § 1.104. Presently withdrawn claims 10, 12-14 and 16-18 depend

directly from product claims 3 and 7. Hence, rejoinder of the withdrawn claims is respectfully requested.

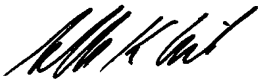
Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all currently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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